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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/393,023	09/09/1999	PAUL S. MEISSNER	PF-200	2146

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EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

[redacted]

Office Action Summary	Application No.	Applicant(s)	
	09/393,023	MEISSNER ET AL.	
	Examiner	Art Unit	
	Lorraine Spector	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,16 and 19-95* is/are pending in the application.

4a) Of the above claim(s) *14,16,19 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *14, 16, 19-95* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 14, 16 and 19-95 are pending.

The restriction requirement mailed 6/19/02 (paper number 23) is withdrawn. Accordingly, the petition filed 9/23/02 (paper number 26) is moot. Claims 14, 16 and 19-20 remain withdrawn from consideration as being drawn to a non-elected invention, election having been made with traverse in paper number 10, filed 5/17/01.

Claims 21-95 are under consideration.

The terminal disclaimer filed on 3/26/02 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 5,981,215 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Objections and Rejections under 35 U.S.C. §§101 and 112

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 21-95 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

The utility set forth in the specification p.17, last paragraph, is that of pancreatic cancer diagnosis. This is based on "An initial Northern blot analysis [that] has shown very high expression in pancreatic cancer cells." For several reasons this is not a specific or substantial utility. First, it is not know how the level of expression compares to expression in normal

noncancerous cells, nor if the expression was analyzed in cell cultures or in cancerous tissue. Markers for cell lines are not necessarily representative of primary cell cultures or tissue since it is well known that cells can undergo changes in expression when cultured for extended passages. Also, a cancer cell line is representative of only a single sample (cell lines originate from one patient's cells), which is not enough information to conclude that protein alteration in that cell line is a universal phenomenon in all or most pancreatic cell samples. Second, polynucleotide expression is not necessarily indicative of protein expression. There is no information on altered level of protein (the claimed product) in pancreatic cancer cells.

The specification teaches that the mature criptin protein (amino acids 24-223 of SEQ ID NO:2) has the putative activity of wound healing and stimulation of vasculogenesis (p. 18,3rd and 4thfull paragraph). The prior art teaches a structurally related protein called "cripto" which has been identified as a cancer marker (p. 2, third paragraph; and references AA and AE), as well as a related gene called "CR-3" (AB), the function of which is also unknown. Neither of these prior art proteins is disclosed as having a transmembrane domain, although criptin is disclosed as having a transmembrane domain (p. 4, 8 lines from bottom). In the current instance the nature the invention is largely unknown since the related prior art proteins have no described function except as tumor cell markers and have a conserved "EGF motif" which confers some structural form. There are no examples of criptin promoting would healing or vasculogenesis. The list of tissue in which it may promote would healing is diverse: skin, bone, muscle, lung..., and no specific tissue is identified nor under what circumstances criptin can actually promote wound healing (*e.g.*, cellular state of tissue--proliferating or differentiating, effective amount, or *in vivo* compared to *in vitro* activity). Also, the currently claimed protein has several putative functions listed and a putative three dimensional structure, but without information on the relationship of structure to function. Therefore, the specification merely proposes possible functions (e.g. "wound healing" for the claimed proteins, none of which would be considered to be credible by the person of ordinary skill in the art in the absence of any characterization as to specific activities and cell types on which the protein might have activity.

Utility must be in readily available form. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because

the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polypeptide which has undetermined function or biological significance. Until some actual and specific activity can be attributed to the protein identified in the specification as criptin, the claimed invention is incomplete. Merely using the protein or polypeptide fragments thereof to further characterize the protein or determine possible diagnostic applications does not constitute a patentable utility.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-95 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 21, 29-33, 35-38 and 41-83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection has two

components: there are new matter issues, and additionally there are issues of a lack of written description of the invention in the specification as originally filed.

New Matter: It is noted that this application is a divisional of the application that issued as U.S. Patent Number 5,981,215. In a preliminary amendment filed 12/8/99, paper number 3, an amended sequence was introduced, based upon a resequencing of the deposited clone. The changes in sequence relative to SEQ ID NO: 2 are a single substitution at residue 36, and complete sequence divergence beginning at residue 186. Thus, residues 186-230 of the issued patent are no longer present, and are replaced by residues 186-223 of the current SEQ ID NO:2. This, in and of itself, is *not* new matter, as the clone had been deposited, and the corrected sequence has been stated to correspond to the deposited clone. However, three of the specifically claimed fragments *do* constitute new matter: The fragment 68-223 of SEQ ID NO:2 is not an originally disclosed fragment. The specification as originally filed claimed a fragment of 68-173, but there appears to be no basis for 68-223, nor for 68 to the terminus of the protein. Fragment 129-207 of SEQ ID NO:2 was originally claimed in claim 30, part (e) of the patent. However, as the current SEQ ID NO: 2 diverges from the SEQ ID NO: 2 of the patent, this is not the same fragment originally disclosed, nor are there any conserved structural features in this region that would serve as a 'landmark' as to the identity of the fragment. Accordingly, the Examiner concludes that there is no evidence of conception of the currently claimed fragment of residues 129-207 of SEQ ID NO: 2 in the specification as originally filed, and such is new matter. Similarly, the fragment 173-223 of SEQ ID NO: 2 can most closely be said to correspond to the previously claimed fragment 173-230 of the previous SEQ ID NO: 2. However, as only the first 13 residues of the originally claimed 57-residue fragment remain, and

the rest of the sequence cannot be said to have been contemplated at the time of filing, the fragment as it is not claimed constitutes new matter.

Lack of written description of the claimed invention in the specification as originally filed: In addition to the above, numerous of the claims, for example claim 32, are drawn to fragments of SEQ ID NO: 2 wherein the fragment 'stimulates cell growth'. There is no disclosure in the specification as originally filed of the concept of fragments that stimulate cell growth, nor is there description of what type of cell growth (i.e. what types of cells) would be so stimulated. Without knowing that the protein has cell-growth stimulatory activity, or what types of cells it would have such activity for, the specification fails to convey conception of fragments which retain such activity.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the full-length SEQ ID NO: 2 and specific fragments of parts a-g of claim 21, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37, 45, 47-69, 72, 74-80, 83, 85, 89, 91 and 95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims such as claim 37 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the means by which the protein can be produced. There is nothing to indicate the host cell anything by which it can produce the protein, for example, a nucleic acid encoding the protein. It is not clear whether the host cell has been transformed with a nucleic acid that encodes the desired protein, or alternatively whether the host cell naturally makes the protein (and its being a 'host' is irrelevant to the method). Further, in step (b), it is unclear if "the protein" recovered is said isolated protein of claim 21 or if it is another protein in/from the cell. Claims 45, 72, 83, 89 and 95 are similarly indefinite.

Claims which recite "The isolated protein of claim x which further comprises", and then go on to recite a further limitation within the metes and bounds of the base claim, such as claims

47-68, are indefinite because, using claim 47 as an example, it is not clear whether applicants intend that there be a second sequence meeting the further limitation fused to the first, or whether applicants actually intend the dependent claim to further limit the first sequence. Claims 74-79 are similarly indefinite.

Claim 69 is indefinite because claim 46, from which it depends, uses the term "amino acid sequence" twice, to refer both to the claimed subject matter and that to which it is compared; it is not clear to which occurrence claim 69 is intended to refer. Claim 80 is similarly indefinite, as are claims 85 and 91; it is not clear whether applicants intend to separate (and potentially discontiguous) fragments, or simply that the fragment is at least 50, and not 30 residues' long.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector, Ph.D.
Primary Examiner

1/2/03

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